

AMENDMENTS TO THE CLAIMS

The following listing of the claims replaces all prior versions of the claims presented in the application.

1. (Original) A recombinant allergen, characterised in that it is a mutant of a naturally occurring allergen, wherein the mutant allergen has at least four primary mutations, which each reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen, wherein each primary mutation is a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, wherein each primary mutation is spaced from each other primary mutation by at least 15 Å, and wherein the primary mutations are placed in such a manner that at least one circular surface region with an area of 800 Å² comprises no mutation.

2. (Previously presented) A recombinant allergen according to claim 1, wherein the primary mutations are spaced between about 20 to 30 Å.

3. (Previously presented) A recombinant allergen according to claim 1 comprising a number of secondary mutations, which each reduce the specific IgE binding capability of the mutated allergen as compared to the binding capability of the said naturally occurring allergen, wherein each secondary mutation is a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, wherein the secondary mutations are placed outside the said circular region.

4. (Previously presented) A recombinant allergen according to claim 1, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 20 %.

5. (Previously presented) A recombinant allergen according to claim 1, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is

conserved with more than 70 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

6. (Previously presented) A recombinant allergen according to claim 1, which essentially has the same α -carbon backbone tertiary structure as said naturally occurring allergen.

7. (Previously presented) A recombinant allergen according to claim 1, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic genus from which said naturally occurring allergen originates.

8. (Previously presented) A recombinant allergen according claim 1, characterised in that the specific IgE binding to the mutated allergen is reduced by at least 5%.

9. (Original) A recombinant allergen according to claim 6, characterised in that when comparing the α -carbon backbone tertiary structures of the mutant and the naturally occurring allergen molecules, the average root mean square deviation of the atomic coordinates is below 2 \AA .

10. (Previously presented) A recombinant allergen according to claim 1, characterised in that said circular surface region comprises atoms of 15-25 amino acid residues.

11. (Previously presented) A recombinant allergen according to claim 1, characterised in that the surface-exposed amino acid residues are ranked with respect to solvent accessibility, and that one or more amino acids among the more solvent accessible ones are substituted.

12. (Previously presented) A recombinant allergen according to claim 1, characterised in that the surface-exposed amino acid residues are ranked with respect to degree of conservation in all known homologous proteins within the species from which said naturally occurring allergen originates, and that one or more amino acids among the more conserved ones are substituted.

13. (Previously presented) A recombinant allergen according to claim 1, wherein the mutant allergen is a non-naturally occurring allergen.

14. (Previously presented) A recombinant allergen according to claim 1 comprising from 5 to 20 primary mutations.

15. (Previously presented) A recombinant allergen according to claim 3 characterised in that the mutant allergen comprises from 1 to 4 secondary mutations per primary mutation.

16. (Previously presented) A recombinant allergen according to claim 1, characterised in that one or more of the substitutions is carried out by site-directed mutagenesis.

17. (Previously presented) A recombinant allergen according to claim 1, characterised in that one or more of the substitutions is carried out by DNA shuffling.

18. (Previously presented) A recombinant allergen according to claim 1, characterised in that it is a mutant of an inhalation allergen.

19. (Original) A recombinant allergen according to claim 18, characterised in that it is a mutant of a pollen allergen.

20. (Original) A recombinant allergen according to claim 19 characterised in that it is a mutant of a pollen allergen originating from the taxonomic order of Fagales, Oleales or Pinales.

21. (Original) A recombinant allergen according to claim 20, characterised in that it is a mutant of Bet v 1.

22. (Currently amended) A recombinant allergen according to claim 21, characterised in that one or more of the substitutions is selected from the group consisting of V2, D72, E87, K-129, E-60, N-7, V-2, D-72, E-87, K-129, E-60, N-7, K-65, P-108, N-159, D-93, K-123, K-32, D-125, R-145, D-109, E-127, Q-36, E-131, L-152, E-6, E-96, D-156, P-63, H-76, E-8, K-134, E-45, T-10, V-12, K-20, S-155, H-126, P-50, N-78, K-119, V-2, L-24, E-42, N-4, A-153, I-44, E-138, G-61, A-130, R-70, N-28, P-35, S-149, K-103, Y-150, H-154, N-43, A-106, K-115, P-14, Y-5, K-137, E-141, E-87 and E-73.

23 and 24. (Canceled)

25. (Original) A recombinant allergen according to claim 18, characterised in that it is a mutant of a house dust mite allergen.

26. (Original) A recombinant allergen according to claim 25, characterised in that it is a mutant of a mite allergen originating from Dermatophagoides.

27. (Canceled)

28. (Original) A recombinant allergen according to claim 18, characterised in that it is a mutant of an animal allergen.

29-34. (Canceled)

35. (Previously presented) A pharmaceutical composition comprising the recombinant allergen according to claim 1 and at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant.

36. (Canceled)

37. (Currently amended) A composition comprising two or more recombinant mutant allergens variants according to claim 1, wherein each of said two or more recombinant mutant allergens comprises variant is defined by having at least one primary mutation that is not within a radius of 15 Å from a secondary mutation and which is, which is absent in at least one other of said two or more recombinant mutant allergens. of the other variants, wherein for each variant no secondary mutation is present within a radius of 15 Å from each absent primary mutation.

38. (Previously presented) A composition according to claim 37 comprising 2-12 variants.

39. (Previously presented) A composition according to claim 37 further comprising at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant.

40-63. (Canceled)

64. (Previously presented) A recombinant allergen according to claim 1 comprising at least one T cell epitope capable of stimulating a T cell clone or T cell line specific for the naturally occurring allergen.

65. (Canceled)

66. (Original) The recombinant allergen of claim 2 wherein the primary mutations are spaced by at least 25 Å.

67. (Original) The recombinant allergen of claim 66 wherein the primary mutations are spaced by at least 30 Å.

68. (Original) The recombinant allergen according to claim 4, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 30 %.

69. (Original) The recombinant allergen according to claim 68, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 40 %.

70. (Original) The recombinant allergen according to claim 69, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 50 %.

71. (Original) A recombinant allergen according to claim 5, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 80 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

72. (Original) A recombinant allergen according to claim 71, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 90 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

73. (Original) A recombinant allergen according to claim 7, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic subfamily from which said naturally occurring allergen originates.

74. (Original) A recombinant allergen according to claim 73, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic family from which said naturally occurring allergen originates.

75. (Original) A recombinant allergen according to claim 74, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the

amino acid sequence of any known homologous protein within the taxonomic superfamily from which said naturally occurring allergen originates.

76. (Original) A recombinant allergen according to claim 75, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic legion from which said naturally occurring allergen originates.

77. (Original) A recombinant allergen according to claim 76, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic suborder from which said naturally occurring allergen originates.

78. (Original) A recombinant allergen according to claim 77, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic order from which said naturally occurring allergen originates.

79. (Original) A recombinant allergen according claim 8, characterised in that the specific IgE binding to the mutated allergen is reduced by at least 10%.

80. (Original) A recombinant allergen according to claim 14 comprising from 6 to 15 primary mutations.

81. (Original) A recombinant allergen according to claim 80 comprising from 7 to 12 primary mutations.

82. (Original) A recombinant allergen according to claim 81 comprising from 8 to 10 primary mutations.

83. (Original) A composition according to claim 38 comprising 3-10 variants.

84. (Original) A composition according to claim 83 comprising 4-8 variants.

85. (Original) A composition according to claim 84 comprising 5-7 variants.